UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	30

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/875,849	Briskin et al.
Examiner	**Art Unit**
Ron Schwadron, Ph.D.	1644

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on 3/2/2001, 11/6/2000 and 3/3/2000

2a) X This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *24-26, 28-34, 37, 38, 44, 46, and 89-135* is/are pending in the application.

4a) Of the above, claim(s) 33, 34, 37, 38, 44, 46, 89-101, 117 is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) 24-26, 28-32, 102-116, 118-135 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) X Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) X Information Disclosure Statement(s) (PTO-1449) Paper No(s).
18) ☐ Interview Summary (PTO-413) Paper No(s).
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

1. Applicant's election of the species MAdCAM fusion protein comprising SEQ ID NO:2 and Ig fusion protein in No. 27 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse. See MPEP section § 818.03(a)).

2. Claims 101 and 117 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 27.

3. Claims 24-26,28-32,102-116,118-135 are under consideration.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24-26,28-32,102-116,118-135 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

The instant claims encompass fusion proteins containing primate MAdCAMs from any primate as well as polymorphic or allelic variants of any primate MAdCAM. The specification discloses one amino acid sequence encoding macaque MAdCAM and two different amino acid sequences encoding human MAdCAM. With the exception of the

aforementioned disclosed amino acid sequences, the skilled artisan cannot envision the detailed structure of the encompassed proteins (or fusion proteins containing said protein) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. For example, there is no disclosure in the specification of chimp MAdCAM or baboon MAdCAM or spider monkey MAdCAM or gibbon MAdCAM or rhesus MAdCAM or polymorphic or allelic variants of said primate MADCAMS. Regarding human MAdCAM and polymorphic or allelic variants of said human MAdCAM, there is no disclosure in the specification of human MAdCAM other than that specifically encoded by the two specific amino acid sequences disclosed in the specification. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated protein is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. In the instant case, the specification has provided three amino acid sequences encoding human or macaque MAdCAM. The claimed inventions encompass fusion proteins containing primate MAdCAMs from any primate as well as polymorphic or allelic variants of any primate MAdCAM. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v.

Eli Lilly and Company (CAFC, July 1997) wherein is stated:
"The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

Regarding applicants comments, the instant claims encompass fusion proteins containing primate MAdCAMs from any primate as well as polymorphic or allelic variants of any primate MAdCAM. In addition, it is noted that claims 107-135 are not even restricted to naturally occurring MAdCAM. They encompass any mutant or variant with a minimal property of MAdCAM as per the definition of said term in the specification. Said claims encompass vast untold numbers of nonnaturally occurring seqeunces. With the exception of fusion proteins containing SEQ. ID. NO:2 or 4 or 6, there is no disclosure of the amino acid sequences of other primates or primate polymorphic or allelic variants or non-naturally occurring mutants. Said seqeunces include two sequences derived from human and one sequence derived from a single species of macaque. According to WWW.blarg.com (found by searching Anthropoidea on DOGPILE search engine), there are 11 families, 52 genera and 181 species encompassed by the term primate. Thus, applicant has not provided a description of the vast majority (eg. 179 of 181) of the amino acid seqeunces which encode primate MAdCAM. Furthermore, this figure does not even take into account naturally occurring polymorphic or allelic variants. If each species had multiple alleles or polymorphic variants than the potential number of MAdCAM seqeunces would vastly increase from the 181 seqeunces number. There is no disclosure in the specification of amino acid seqeunces encoding MAdCAM derived from the primates tufted ear marmoset, mantled howler, brown headed spider monkey, dusky titi, the patas

monkey, savanna baboon, haunman langur, the black han gibbon, the bonobo, etc. Applicants disclosure is a minuscule fragment of the potential MAdCAMs derived from species encompassed by the term primate. Regarding applicants comments about claims that recite 55% similar, etc., in view of the fact that said claims do not specify what particular regions of the sequence are similar and do not specify the identity of the 45% nonsimilar portion, it is unclear as to how this provides a further description of the seqeunce encoding other primate variants. In addition, it is noted that claims 113-135 are not even restricted to naturally occurring MAdCAM. They encompass any mutant or variant with a minimal property of MAdCAM as per the definition of said term in the specification. Said claims encompass vast untold numbers of nonnaturally occurring seqeunces. Attention is directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated:

"The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

6. Claims 107-113,121-135 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the fusion proteins of claims 107-112,120-135. Said claims recite that the fusion protein contains an $\alpha 4\beta 7$ integrin-binding fragment and wherein said molecule has a particular degree of similarity with a specific amino acid sequence recited in the claim. The claims encompass a sequence that has the recited

sequence similarity and also the functional property of $\alpha 4\beta 7$ integrin-binding. However, there is no disclosure in the specification as to what amino acid residues are important for $\alpha 4\beta 7$ integrin-binding. The claims encompass fusion proteins wherein 45% to 10% of the amino acid sequence has no similarity to the sequence recited in the claim. The art recognizes that even single amino acid change or mutation can destroy the function of the biomolecule in many instances. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence similarity (wherein the entire sequence is not part of the binding domain) results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function. Lederman et al. document this unpredictability of the relationship between sequence and function wherein a single amino acid substitution can ablate receptor/ligand binding. Therefore, it would be unpredictable as to what amino acid seqeunces would or would not have the functional activity recited in the claim. It would require undue experimentation to practice the claimed invention based on the teachings of the specification.

7. Claims 105-112,115,116,120-135 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "nucleic acid that shares at least about 75%(or 90%)" in claims 105,106,115,116. The specification, page 17, line 18 does not disclose said limitation.

There is no support in the specification as originally filed for the fusion protein of claims 107-112,120-135 which contains an $\alpha 4\beta 7$ integrin-binding fragment and wherein the sequence "is at least 55% (or 75% or 90%) similar" or wherein said claim defines said fragment as per claim 108. There is no support for such a claim in the passages of the specification to which applicant refers or original claim 27.

8. Regarding the priority date of the instant application with regards to the application of prior art, the claimed inventions are not disclosed in parent application 08/386857 and

therefore the claimed inventions are not entitled to priority to said application with regards to the application of prior art.

9. Regarding the term "similarity" as recited in the claims, there is no actual definition of said term in the specification. While the specification discloses a particular method that could presumably be used to determine similarity (see page 48, last paragraph), there is no disclosure in the specification that the term similarity does not encompass other forms of similarity. For the purposes of applying prior art, the term could be interpreted as meaning containing the same amino acids irregardless of linear order (eg. both proteins contain all known amino acids, therefore they have 100% similarity).

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 107-111,113-116,118,120-124,126-135 are rejected under 35 U.S.C. 102(b) as being anticipated by Butcher et al. (WO 94/13312).

In the instant rejection the term "similarity" is interpreted as meaning containing the same amino acids irregardless of linear order (eg. both proteins contain all known amino acids, therefore they have 100% similarity). Regarding the term primate or human MAdCAM, if the term "similarity" is interpreted as above and the terms primate or human MAdCAM are interpreted as per paragraph 12 of the Office Action mailed 8/26/99, then the claims would encompass murine MAdCAM. Murine MAdCAM also has 100% similarity to human/primate MAdCAM as per the definition of said term in this rejection. Butcher et al. teach MAdCAM/Ig constant region fusion proteins (see page 7). Murine MAdCAM has a $\alpha 4\beta 7$ integrin-binding fragment. Murine MAdCAM would be a "primate MAdCAM" as this term is defined in the specification. In addition, it also qualifies as a "primate MAdCAM"

because it has numerous properties, activities and functional characteristics of naturally occurring human MAdCAM (eg. both made of amino acids, both mediate adhesion, both found in mammals, both contain carbon and oxygen molecules, etc). Butcher et al. teach that the peptide is joined to IgG, indicating that the c-terminal of said peptide is joined to the N-terminal of Ig (see page 7). Butcher et al. teach soluble MAdCAM (page 5) and fusion molecules containing said peptide (see page 7). The MAdCAM/Ig fusion protein taught by Butcher et al. contains at least a portion of Ig heavy chain constant region (eg. intact IgG, see page 7). It is an inherent property of IgG that it contains hinge, CH2 and CH3 domains because these regions are found in IgG. The fusion protein taught by Butcher et al. is a "hybrid immunoglobulin".

12. Claims 24-26,28-32,102-106,113-116,118,119 are rejected under 35 U.S.C. 102(e) as being anticipated by Capon et al. US Patent 5,565,335.

Regarding the term "naturally occurring primate MAdCAM", the specification discloses said phrase on page 13, lines 3 and 4. Said term refers to a naturally occurring MAdCAM molecule found in primates. The definition of the term "MAdCAM" in the specification, on page 11 , last paragraph indicates MAdCAM encompasses any molecule with at least one property of MAdCAM (eg. mediates cellular adhesion). Thus, a "naturally occurring primate MAdCAM" would encompass primate derived adhesion molecules per se. The issue of "similarity" has been addressed above.

Capon et al. teach immunoadhesion fusion proteins (see claims 1-14). Capon et al. teach an immunoadhesion containing a human molecule (CD4) which can mediate adhesion (see Examples). Said molecule would encompass a "naturally occurring primate MAdCAM" because it is a naturally occurring human molecule with at least one property of MAdCAM (eg, mediates adhesion). Capon et al. teach the claimed fusion proteins (see claims 1-14 and Examples). In the instant rejection the term "similarity" is interpreted as meaning containing the same amino acids irregardless of linear order (eg. both proteins contain all known amino acids, therefore they have 100% similarity). If the term "similarity" if is interpreted as above and the term "naturally occurring primate MAdCAM" is interpreted as above, then human CD4 is a human/primate naturally occurring MAdCAM.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 107-116,118-135 are rejected under 35 U.S.C. 103(a) as being unpatentable over Butcher et al. in view of Capon et al.

In the instant rejection the term "similarity" is interpreted as meaning containing the same amino acids irregardless of linear order (eg. both proteins contain all known amino acids, therefore they have 100% similarity). Regarding the term primate or human MAdCAM, if the term "similarity" is interpreted as above and the terms primate or human MAdCAM are interpreted as per paragraph 12 of the Office Action mailed 8/26/99, then the claims would encompass murine MAdCAM. Murine MAdCAM also has 100% similarity as per the working definition in this rejection. Butcher et al. teach MAdCAM/Ig constant region fusion proteins (see page 7). Murine MAdCAM has a $\alpha 4\beta 7$ integrin-binding fragment. Murine MAdCAM would be a "primate MAdCAM" as this term is defined in the specification. In addition, it also qualifies as a "primate MAdCAM" because it has numerous properties, activities and functional characteristics of naturally occurring human MAdCAM (eg. both made of amino acids, both mediate adhesion, both found in mammals, both contain carbon and oxygen molecules, etc). Butcher et al. teach that the peptide is joined to IgG, indicating that the c-terminal of said peptide is joined to the N-terminal of Ig (see page 7). Butcher et al. teach soluble MAdCAM (page 5) and fusion molecules containing said peptide (see page 7). The MAdCAM/Ig fusion protein taught by Butcher et al. contains at least a portion of Ig heavy chain constant region (eg. intact IgG, see page 7). It is an inherent property of IgG that it contains hinge, CH2 and CH3 domains because these regions are found in IgG. The fusion protein taught by Butcher et al. is a "hybrid immunoglobulin". Butcher et al. do not teach an Ig fusion protein heterodimer. Capon et al. teach Ig fusion protein heterodimers (see claim 8). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Butcher et al. teach the claimed invention except for an Ig fusion protein heterodimer, while Capon et al. teach Ig fusion protein

heterodimers. One of ordinary skill in the art would have been motivated to do so because heterodimeric fusion proteins have a variety of art recognized uses (eg. could be used in immunoassays, etc.).

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Papers related to this application may be submitted to Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1640 at (703) 305-3014.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1640 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1800

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644